UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/031,691	04/18/2002	Victor Uebele	20499P	8269

210 7590 10/22/2004

MERCK AND CO INC
P O BOX 2000
RAHWAY, NJ 070650907

EXAMINER	
MERTZ, PREMA MARIA	
ART UNIT	**PAPER NUMBER**
1646	

DATE MAILED: 10/22/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/031,691	UEBELE ET AL.	
	Examiner	Art Unit	
	Prema M Mertz	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *8/20/2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-42* is/are pending in the application.

4a) Of the above claim(s) *13 and 15-42* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-12, 14* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Restriction/Election

1. Applicant's election with traverse of Group I (claims 1-12, 14) on 8/20/04 is acknowledged. The traversal is on the ground(s) that the restriction is improper because Group I (drawn to a DNA molecule encoding a protein of SEQ ID NO:2) and Group VI (drawn to an antibody to a protein of SEQ ID NO:2) should be grouped together. Further, Applicants argue that Group II (drawn to a DNA molecule encoding a protein of SEQ ID NO:4) and Group VII (drawn to an antibody to a protein of SEQ ID NO:4) should be grouped together and so should DNA and proteins of Groups III-V and VIII-X. However, Applicants arguments with respect to including the antibody of Group VI with elected Group I is not found to be persuasive because contrary to Applicants arguments, the special technical feature of the invention encompassing the DNA encoding the polypeptide of SEQ ID NO:2, is the amino acid sequence of SEQ ID NO:2. The antibody to SEQ ID NO:2 does not share this special technical feature because the antibody is structurally and functionally different from the polypeptide and examination of both these inventions would place undue examination burden on the Examiner.

Furthermore, contrary to Applicants arguments, there is no unity of invention between Groups II-V (proteins) and Groups VII-X (antibodies to the proteins) because these are structurally and functionally different compounds and a search for one protein would not reveal art pertinent to another protein or an antibody to the protein. Distinctness is further shown because each of these products can be made and used without any one or more of the other products. The products in the different Groups are physically, chemically and biologically distinct from each other, and if patentable would

support separate patents. Furthermore, separate search terms would be required for searching the literature, and a search of the literature for one protein would not necessarily reveal art for another.

The test for propriety of restriction is not whether the inventions are related but rather whether they are distinct and whether it would impose a burden on the examiner to search and examine multiple inventions in a single invention. The different polypeptides and antibodies are related as different products, which are independent and distinct, each from the other, which possess characteristic differences in structure and each has an independent utility, that is distinct for each invention which cannot be exchanged.

Lastly the inventions are distinct because a search of the literature for the polypeptide of SEQ ID NO:2 and the polynucleotide encoding said polypeptide, would not be expected to reveal art for all the other polypeptides of SEQ ID NO:4, 6, 8, 10, which searches are extensive requiring separate searches, which would be unduly burdensome.

The Groups as delineated in the restriction requirement (7/23/04) are patentably distinct one from the other such that each invention could, by itself, in principle, support its own separate patent (as shown by the arguments put forth in the written restriction requirement).

The requirement is still deemed proper and is therefore made FINAL.

Claims 1-12 and 14 encompassing polynucleotides encoding polypeptides set forth in SEQ ID NO: 4, 6, 8, 10 and the polypeptides encoded thereby, as well as claims 13, 15-42, are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

Specification

2. In the first line of the instant specification, under "Cross Reference to related Application", Applicants are requested to update the status of the prior provisional application 60/144,764 to which the instant application is claiming benefit.

3. The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed. Furthermore, all inventions are presumed novel. Therefore, it is suggested that the term "novel" be deleted from the title of the invention.

Claim Rejections - 35 USC § 101

4. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter or any new and useful improvement thereof, may obtain a patent therefore, subject to the conditions and requirements of this title.

Claim 12 is rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter.

The claim embraces a naturally occurring protein in a host. However, since it would that applicants do not intend to claim such proteins, amending the claim to require the hand-of-man would obviate this rejection i.e. an isolated protein.

Claim rejections-35 USC § 112

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5a. Claims 1, 5-8, are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an isolated DNA encoding a protein comprising the amino acid sequence set forth in SEQ ID NO:2 and the protein encoded thereby, does not reasonably provide enablement for an isolated DNA encoding a human calcium sensitive potassium channel β2 protein and a human calcium sensitive potassium channel β2 protein. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Claim 8, for example, is clearly a single means claim because it encompasses any human calcium sensitive potassium channel β2 protein that exists now and in the future, irrespective of the structure of that protein. Claim 8 is a single means claim because the specification has only provided a description for a polypeptide of amino acid sequence set forth in SEQ ID NO:2. A single means claim, i.e., where a means recitation does not appear in combination with another recited element of means, is subject to an undue breadth rejection under 35 U.S.C. 112, first paragraph. *In re Hyatt*, 708 F.2d 712,714 - 715, 218 USPQ 195, 197 (Fed. Cir. 1983) (A single means claim which covered every conceivable means for achieving the stated purpose was held nonenabling for the scope of the claim because the specification disclosed at most only those means known to the inventor.). When claims depend on a recited property, a fact situation comparable to Hyatt is possible, where the claim covers every conceivable structure (means) for achieving the stated property (result) while the specification discloses at most only those known to the inventor. See M.P.E.P. 2164.08(a).

The instant specification is not enabling for the scope of the claims because one cannot following the guidance presented therein produce the claimed antibody to a protein comprising the amino acid sequence of SEQ ID NO:2 without first making a substantial inventive contribution.

5b. Claims 1, 5-11 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an isolated DNA encoding a protein comprising the amino acid sequence set forth in SEQ ID NO:2 and the protein of amino acid sequence set forth in SEQ ID NO:2, does not reasonably provide enablement for "all" human calcium sensitive potassium channel β2 proteins or muteins of a protein of amino acid sequence set forth in SEQ ID NO:2 as recited in claims 10-11. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The specification delimits the instant protein by reference to specific amino acid arrays as set forth in SEQ ID NO:2, however, in claims 1 and 8, the protein is defined by reference to the abbreviation β2 protein, wherein the abbreviation itself does not represent any distinguishing information concerning the disclosed protein. Moreover because β2 protein does not inherently correspond to any particular protein, claims that lack the recitation of structural properties encompass subject matter not supported by the instant specification. Molecules that are embraced by the claims are not adequately supported by the instant specification because the specification provides no guidance for how to make such molecules nor are examples provided as to how these molecules would be identified commensurate with the breadth of the claims. In the absence of an

appropriate structural and/or functional reference, a person of ordinary skill in the art would be unable to make and use the molecules embraced by the claims without undue experimentation because one could not distinguish the proteins envisaged by the specification and those, which are unrelated.

With respect to claims 1, 8, as recited, what is claimed in the instant invention broadly encompasses "all" human calcium sensitive potassium channel β2 proteins. While the specification discloses the human calcium sensitive potassium channel β2 protein activity in Figure 7 and this is the biological property which the polypeptide is expected to exhibit, the specification is non-enabling for the unlimited number of compositions comprising human calcium sensitive potassium channel β2 proteins, and which are encompassed by the scope of the claims. The claimed invention encompasses compositions not envisioned or described in the specification, and neither does the specification disclose how these claimed compositions can be distinguished from each other. The specification only enables a protein having the amino acid sequence shown in SEQ ID NO:2, the polypeptide having specific characteristics and properties. These properties may differ structurally, chemically and physically from other known proteins. By application of the factors set forth in Ex parte Forman (230 USPQ 546 (Bd. Pat. App. & Int. 1986), and reiterated in In re Wands (858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)), which include (1) quantity of experimentation, (2) guidance presented, (3) the predictability of the art, and (4) the breadth of the claims, in the instant application, the quantity of experimentation to determine which other proteins are encompassed by the scope of the claims is practically infinite and the guidance provided in the specification very little, thereby rendering the results of the assays taught in the

specification unpredictable (see pages 51-52, Example 2). Therefore, it would require undue experimentation to determine which proteins having the biological activity of human calcium sensitive potassium channel β2 proteins, would be encompassed by the scope of the claims. The disclosure of a natural polypeptide is clearly insufficient support under the first paragraph of 35 U.S.C. § 112 for claims, which encompass every and all polypeptides, including mutants thereof. In In re Fisher, 427 F.2d 833, 166 USPQ 18 (CCPA 1970), the Courts have held that:

"Inventor should be allowed to dominate future patentable inventions of others where those inventions were based in some way on his teachings, since some improvements while unobvious from his teachings, are still within his contribution, since improvement was made possible by his work; however, he must not be permitted to achieve this dominance by claims which are insufficiently supported and hence, not in compliance with first paragraph of 35 U.S.C. 112; that paragraph requires that the scope of the claims must bear a reasonable correlation to scope of enablement provided by specification to persons of ordinary skill in the art; in cases involving predictable factors, such as mechanical or electrical elements, a single embodiment provides broad enablement in the sense that, once imagined, other embodiments can be made without difficulty and their performance characteristics predicted by resort to known scientific law; in cases involving unpredictable factors, such as most chemical reactions and physiological activity, scope of enablement varies inversely with degree of unpredictability of factors involved."

Furthermore, the amount of embodiments corresponding to the desirable compositions, may be innumerable, and the enabled embodiments amount to only one.

Therefore, there are substantial scientific reasons to doubt the scope of enablement, as set forth above. Reasonable correlation must exist between the scope of the claims and scope of enablement set forth. The specification does not describe any other polypeptide other than that whose amino acid sequence is shown in SEQ ID NO:2, and since it is deemed to constitute undue experimentation to determine all the others, the disclosure is not commensurate with the scope of the claims. Therefore, Applicants are not enabled for a protein having anything less than the amino acid sequences shown in SEQ ID NO:2. It is suggested that by employing conventional claim language, the claims be amended to include the specific polypeptide supported by the instant specification.

Furthermore, with respect to claim 12, the instant specification fails to adequately describe and enable an isolated protein that is at least 80% identical to the polypeptide of SEQ ID NO:2. Applicants do not teach which regions of said polypeptide are critical to encode a functional polypeptide. The specification does not provide the requisite examples nor a representative number of different sequences that would allow the skilled artisan to produce a polypeptide having at least 80% sequence identity to SEQ ID NO:2, nor does the disclosure provide criteria that explicitly enable such critical features. There is no guidance in the specification as to how one of ordinary skill in the art would generate a polypeptide, other than that exemplified. The issue here is the breadth of the claim in light of the predictability of the art as determined by the number of working examples, the skill level of the artisan and the guidance presented in the instant specification and the prior art of record.

In summary, the amount of experimentation required for one of ordinary skill in the art to use the claimed invention, an isolated polypeptide that is at least 80% identical

to the polypeptide of SEQ ID NO:2, would be undue. To practice the instant invention in a manner consistent with the breadth of the claims would not require just a repetition of the work that is described in the instant application but a substantial inventive contribution on the part of a practitioner which would involve the determination of those nucleotide sequences of the disclosed naturally-occurring nucleic acid encoding the claimed polypeptide, which are required for functional and structural integrity of the claimed polypeptide. It is this additional characterization of the disclosed polypeptide that is required in order to obtain the functional and structural data needed to permit one to produce a polypeptide which meets both the structural and functional requirements of the instant claim that constitutes undue experimentation.

With respect to claims 10-11, which recite non-conserved amino acid substitutions, the issue here is the breadth of the claims in light of the predictability of the art as determined by the number of working examples, the skill level of the artisan and the guidance presented in the instant specification and the prior art of record. This position is consistent with the decisions in In re Fisher, 427 F.2d 833, 166 USPQ 18 (CCPA 1970) and Amgen Inc. V. Chugai Pharmaceuticals Co. Ltd., 13 USPQ2d, 1737 (1990), and In re Wands, 8USPQ2d, 1400 (CAFC 1988) (which has been cited by Applicants. If Applicants will kindly review page 1404 of In re Wands, they will find that the factors to be considered in determining whether a disclosure would require undue experimentation include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art and (8) the breadth of the claims.

Further, In re Wands determined that the repetition of work which was disclosed in a patent application as producing a composition containing an antibody, which is a naturally-occurring compound, did not constitute undue experimentation even if the antibody produced thereby was not identical to those that were disclosed in that application. The instant claims are not limited to naturally-occurring compounds and the instant specification does not provide a description of a repeatable process of producing protein whose amino acid sequence deviates from SEQ ID NO:2 by two or more (no upper limit) amino acid substitutions. To practice the instant invention in a manner consistent with the breadth of the claims would not require just a repetition of the work that is described in the instant application but a substantial inventive contribution on the part of a practitioner which would involve the determination of those amino acid residues of the disclosed naturally-occurring protein, which are required for functional and structural integrity of those proteins. It is this additional characterization of the disclosed protein that is required in order to obtain the functional and structural data needed to permit one to produce a protein, which meets both the structural and functional requirements of the instant claims that constitutes undue experimentation.

Furthermore, Applicant is encouraged to review the discussion of 35 U.S.C. § 112, first paragraph, in a recent CAFC decision, Genentech, Inc. v. Novo. Nordisk, 42 USPQ2d, 100 (CAFC 1997), in which the decisions in In re Fisher, Amgen Inc. V. Chugai Pharmaceuticals Co. Ltd., and In re Wands were considered as the controlling precedents in determining enablement issues where protein and recombinant DNA issues are concerned. These decisions have been relied upon in the instant rejection and by the Court because they show that the judicial interpretation of the first paragraph of 35

U.S.C. § 112 requires that the breadth of claims must be based upon the predictability of the claimed subject matter and not on some standard of trial and error. To argue that one can make material embodiments of the invention and then test for those that work in the manner disclosed or that the instant claims only encompass the working embodiments is judicially unsound. Unless one has a reasonable expectation that any one material embodiment of the claimed invention would be more likely than not to function in the manner disclosed or the instant specification provides sufficient guidance to permit one to identify those embodiments which are more likely to work than not, without actually making and testing them, then the instant application does not support the breadth of the claims. In the instant case it is highly improbable that a protein having amino acid substitutions recited in claim 11 will more likely than not perform in the manner disclosed and the instant specification does not provide the guidance needed to predictably alter SEQ ID NO:2 with any reasonable expectation that the resulting protein will have the desirable activity set forth in Figure 7.

6. Claims 1, 5-11, are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The written description in this case only sets forth SEQ ID NO:2 and equivalent degenerative codon sequences thereof and therefore the written description is not commensurate in scope with the claims drawn to a DNA encoding a human calcium sensitive potassium channel β2 protein as recited in claim 1, variants of the protein as recited in claims 10-11 and the protein as recited for example in claim 8.

Vas-Cath Inc. V. Mahurkar, 19 USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed*." (See page 1117). The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (*See Vas-Cath* at page 1116). Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 USC 112 is severable from its enablement provision (see page 115).

The instant specification does not provide an adequate description of the genus of DNA and protein molecules encompassed by these claims. In the decision of *The Regents of the University of California v. Eli Lilly and Company,* 43 USPQ2d 1398 (CAFC 1997), the court held that:

"To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention." *Lockwood v. American Airlines, Inc.*, 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (1997); *In re Gosteli*, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989) (" [T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed."). Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." *Lockwood*, 107 F.3d at 1572, 41 USPQ2d at 1966.

An adequate written description of a DNA, such as the cDNA of the recombinant plasmids and microorganisms of the '525 patent, "requires a precise definition, such as

by structure, formula, chemical name, or physical properties," not a mere wish or plan for obtaining the claimed chemical invention. *Fiers v. Revel*, 984 F.2d 1164, 1171, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993). Accordingly, "an adequate written description of a DNA requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it; what is required is a description of the DNA itself." Id. at 1170, 25 USPQ2d at 1606. The instant specification does not provide a structural formula which is definitive of a genus of human calcium sensitive potassium channel β2 proteins and the DNA encoding such proteins. A patent is granted for a completed invention, not the general suggestion of an idea and how that idea might be developed into the claimed invention. In the decision of *Genentech, Inc, v. Novo Nordisk*, 42 USPQ 2d 100,(CAFC 1997), the court held that "[p]atent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable" and that "[t]ossing out the mere germ of an idea does not constitute enabling disclosure". The court further stated that "when there is no disclosure of any specific starting material or of any of the conditions under which a process is to be carried out, undue experimentation is required; there is a failure to meet the enablement requirements that cannot be rectified by asserting that all the disclosure related to the process is within the skill of the art", "[i]t is the specification, not the knowledge of one skilled in the art, that must supply the novel aspects of an invention in order to constitute adequate enablement".

Thus, the structure of the DNA molecules encoding human calcium sensitive potassium channel β2 variants and the variants encoded thereby are not defined. With the exception of SEQ ID NO:2 and SEQ ID NO:1, the skilled artisan cannot envision the

detailed structure of the encompassed polynucleotides and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and a reference to a potential method of isolating it. The nucleic acid itself is required. See *Fiers v. Revel*, 25 USPQ 2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. V. Chugai Pharmaceutical Co. Lts.*, 18 USPQ2d 1016.

Furthermore, In *The Regents of the University of California v. Eli Lilly* (43 USPQ2d 1398-1412), the court held that a generic statement, which defines a genus of nucleic acids by only their functional activity does not provide an adequate written description of the genus. The court indicated that while Applicants are not required to disclose every species encompassed by a genus, the description of a genus is achieved by the recitation of a representative number of DNA molecules, usually defined by a nucleotide sequence, falling within the scope of the claimed genus. At section B(1), the court states that "An adequate written description of a DNA...'requires a precise definition, such as by structure, formula, chemical name, or physical properties', not a mere wish or plan for obtaining the claimed chemical invention".

Furthermore, there is no disclosure of variants of a human calcium sensitive potassium channel β2 protein or the DNA encoding such in the specification. This is insufficient to support the generic claims as provided by the Interim Written Description Guidelines published in the June 15, 1998 Federal Register at Volume 63, Number 114, pages 32639-32645.

Therefore only an isolated nucleic acid molecule comprising a nucleic acid sequence consisting of SEQ ID NO:1 and equivalent degenerative codon sequences thereof, but not the full breadth of the claims meets the written description provision of 35 USC 112, first paragraph.

7. Claim 14 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The written description in this case only sets forth SEQ ID NO:1 and equivalent degenerative codon sequences thereof and therefore the written description is not commensurate in scope with the claims drawn to a DNA or RNA comprising at least 15 contiguous nucleotides of SEQ ID NO:1 as recited in claim 14.

Claim 14 recites the limitation "comprising at least 15 contiguous nucleotides" and encompasses a genus of nucleic acid molecules comprise only portions of the full-length sequence of SEQ ID NO:1 as well as variants having one or more nucleotide deletions, insertions and/or additions made to SEQ ID NO: 1. The specification and claim do not indicate what are the distinguishing attributes shared by the members of the genus for which the common portion is responsible for functional activity. The specification and claim do not place any limit on the number of nucleotides that may be added to the portions since the claim is not limited to the full-length SEQ ID NO:1. Thus, the claim encompasses numerous structural variants, and the genus is highly variant because a significant number of structural differences between genus members is permitted. The specification and claim do not provide a written description as to what changes should be

made. Structural features that could distinguish compounds in the genus from others in the protein class are missing from the disclosure. No common structural and functional attributes identify the members of the genus. The general knowledge and level of skill in the art do not supplement the omitted description because specific, not general, guidance is what is needed. Since the disclosure fails to describe the common attributes or characteristics that identify members of the genus, and because the genus is highly variant, nucleic acid molecules comprising at least 15 contiguous nucleotides of SEQ ID NO:1 alone are insufficient to describe the genus. One of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe the genus. Thus, Applicant was not in possession of the claimed genus.

8. Claim 14 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for as isolated DNA or RNA comprising the nucleotide sequence set forth in SEQ ID NO:1, does not reasonably provide enablement for a DNA or RNA comprising at least 15 contiguous nucleotides of SEQ ID NO:1 as recited in claim 14. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The claimed genus of polynucleotide molecules encompasses variants, however, the specification does not teach how to make a polynucleotide molecule having a nucleotide sequence less than SEQ ID NO:1. The specification only enables a nucleic acid molecule of SEQ ID NO:1, and is not enabled for a nucleic acid molecule of nucleotide sequence anything less than what is disclosed in SEQ ID NO:1.

The issue in the instant case is the breadth of the claims in light of the predictability of the art as determined by the number of working examples, the skill level of the artisan and the guidance presented in the instant specification and the prior art of record. The recitation of "comprising at least 15 contiguous nucleotides... of SEQ ID NO:1" in claim 14, is not a sufficient structural limitation and broadly encompasses any nucleic acid molecule comprising 15 contiguous nucleotide sequences recited in the claim. Because of the presence of the term "comprising" in claim 14, the claim encompasses over 5×10^{100} embodiments.

Furthermore, Applicants have not taught how to make the instant nucleic acid molecules with the stretch of 15 contiguous nucleotides as recited in claim 15. The instant claims are not limited to naturally-occurring compounds and the instant specification does not provide a description of a repeatable process of producing a nucleic acid molecule as claimed.

9. Claim 12 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an isolated polypeptide comprising the amino acid sequence set forth in SEQ ID NO:2, does not reasonably provide enablement for an polypeptide comprising an amino acid sequence with at least 80 % amino acid sequence identity to SEQ ID NO:2. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Claim 12, is overly broad in the recitation of "at least 80% identical to an amino acid sequence" since no guidance is provided as to which of the myriad of polypeptide species encompassed by the claim will retain the desired characteristics. Variants of the

protein can be generated by natural deletions, additions or substitutions of nucleotides, but Applicants have not disclosed any actual or prophetic examples on expected performance parameters of any of the possible muteins of SEQ ID NO:2. There is no guidance provided in the specification as to how one of ordinary skill in the art would generate a nucleic acid sequence encoding a polypeptide other than that exemplified in the specification. See *In re Wands*, 858 F.2d at 737, 8 USPQ2d at 1404. The test of enablement is not whether any experimentation is necessary, but whether, if experimentation is necessary, it is undue. The factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue" include, but are not limited to: (1) the breadth of the claims; (2) the nature of the invention; (3) the state of the prior art; (4) the level of one of ordinary skill; (5) the level of predictability in the art; (6) the amount of direction provided by the inventor; (7) the existence of working examples; and (8) the quantity of experimentation needed to make or use the invention based on the content of the disclosure. Given the breadth of the claims in light of the predictability of the art as determined by the number of working examples, the level of skill of the artisan, and the guidance provided in the instant specification and the prior art of record, it would require undue experimentation for one of ordinary skill in the art to make and use the claimed invention.

Claim rejections-35 USC § 112, second paragraph

10. Claims 1-12 and 14 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 2, 3, 4, 9, 14 are vague and indefinite because they recite non-elected subject matter. Appropriate correction is requested.

Claim 1 is incorrect because it recites "a isolated DNA comprising nucleotides.." rather than "an isolated DNA molecule comprising a nucleotide sequence..".

Claim 5 recites "hybridizes under stringent conditions", which is a relative and conditional term and renders the claim indefinite. Furthermore, some nucleic acids, which might hybridize under conditions of moderate stringency, for example, would fail to hybridize at all under conditions of high stringency. The metes and bounds of the claim thus cannot be ascertained.

Claims 6-8, 10-12, are rejected as vague and indefinite insofar as they depend on the above rejected claims for their limitations.

Claim Rejections - 35 USC § 102

11. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

Claims 1, 4, 5-8, 10-12, 14 are rejected under 35 U.S.C. 102(b) as being anticipated by WO 00/12711.

The reference discloses a 1300 bp cDNA encoding a human membrane channel protein, MECHP-16 protein, and the protein encoded thereby (see abstract, Table 2, page 69, SEQ ID NO:16). A copy of the comparison of SEQ ID NO:1 of the DNA of the instant invention and the DNA disclosed in the reference is enclosed at the end of this action (SEQUENCE COMPARISON A) and demonstrates 99.7% identity. The DNA of

the reference would be capable of hybridizing under stringent conditions to the DNA of SEQ ID NO:1 described in the instant application. The reference also discloses that the cDNA encoding the membrane channel protein was cloned into an expression vector, which contains a promoter operably linked to the cDNA insert encoding the protein, as shown by the ability of the vector to be expressing the protein. Host cells were transformed with the cDNA in the vector (see pages 28-30, 51-52). Therefore, the cDNA and polypeptide disclosed in the reference meets the limitations of claims 1, 4, 5-8, 10-12, 14.

Conclusion

No claim is allowable.

Advisory Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Prema Mertz whose telephone number is (571) 272-0876. The examiner can normally be reached on Monday-Friday from 7:00AM to 3:30PM (Eastern time).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brenda Brumback, can be reached on (571) 272-0961.

Official papers filed by fax should be directed to (703) 872-9306. Faxed draft or informal communications with the examiner should be directed to (571) 273-0876.

Information regarding the status of an application may be obtained from the Patent application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Prema Mertz Ph.D.
Primary Examiner
Art Unit 1646
September 7, 2004